ORAL COMMUNICATIONS / INCORPORATIONS

Thursday, December 7, 2023

1.

EFECTO DE LA PANDEMIA DE COVID-19 SOBRE EL NIVEL DE POLIFARMACIA Y CARGA ANTICOLINÉRGICA EN PERSONAS MAYORES. Effect of the covid-19 pandemic on the level of polypharmacy and anticholinergic burden in elderly people.

Chile is experiencing an accelerated demographic change; the percentage of people aged 60 and over, with respect to the total population, has been increasing progressively. In 1992 this age group was equivalent to 9.5% of the total, in 2022 it increased to 18.1% and it is expected that in 2050 the population of older people will reach 32.1%. The change in the population pyramid is associated with an increase in the life expectancy at birth, reaching 79.5 years in 2022 and projecting 81.2 years for 2023. In this regard, it is important to highlight that an increase in the life expectancy of the elderly also means an increase in pathologies, polypharmacy and anticholinergic burden. Anticholinergic burden is detrimental to cognitive health. Several studies demonstrate that a high anticholinergic burden is associated with an increased risk for dementia and cognitive decline. We evaluated the impact of the Covid-19 pandemic on the polypharmacy and anticholinergic burden in elderly people. This study was carried out in elderly people diagnosed to Chronic Arterial Hypertension, who received services in a center of primary care in Hualpén. The anticholinergic burden was measured for each participant by adding up the anticholinergic scores for individual drugs using the Anticholinergic Cognitive Burden Scale. The anticholinergic burden levels were compared between the pre (n=94) and post (n=46) Covid-19 pandemic groups. Our results demonstrate that in 2018, 65% of the elderly people had polypharmacy with an anticholinergic scores of 17. In 2023, the level of polypharmacy increased to 79% and the anticholinergic scores to 22. We should reinforce existing guidance on reducing overprescribing drugs, limite inappropriate polypharmacy and deprescribing intervention on reducing the anticholinergic burden.

Autores: Sepúlveda, M.J.1; Vásquez, B.1; Chamblás, I.2; Guevara, P.3; Rojas, G.4; Sáez, C.5
Afiliación: 1 Department of Pharmacology, School of Biological Sciences, Universidad de Concepción, Chile. 2 Department of Social Work, School of Social Sciences, Universidad de Concepción, Chile. 3 Department of Electrical Engineering, School of Engineering, Universidad de Concepción, Chile. 4 Department of Informatics and Computer Sciences, School of Engineering, Universidad de Concepción, Chile. 5 Department of Internal Medicine, School of Medicine, Universidad de Concepción, Chile.
Área de la Farmacología: Clinical Pharmacology
Dirección de Correo: jsepulve@udec.cl
Agradecimientos: Proyecto Fondef IT21I0097

2.

ZEBRAFISH COMO UNA HERRAMIENTA EN EL DESCUBRIMIENTO DE DROGAS: EL ROL DE LOS ANTAGONISTAS NICOTÍNICOS EN LA ADICCIÓN A NICOTINA Y ETANOL. Zebrafish as a Tool for Drug Discovery: The Role of Nicotinic Antagonist in Nicotine and Ethanol Addiction.

Nicotinic acetylcholine receptors (nAChR) are part of the family of ion channels activated by ligands. There are several subtypes of nicotinic receptors, given their pentameric nature, among which the α4β2 and α7 subtypes appear to be the most abundant in the Central Nervous System (CNS). They are responsible for the permeability of the cell membrane to sodium and calcium ions, having a relevant function in the central nervous system, modulating the release of different neurotransmitters, such as dopamine and norepinephrine, among others. Nicotinic acetylcholine receptors are associated with mood disorders such as anxiety and abuse of addictive substances such as nicotine and ethanol. Our work has oriented toward the search for molecules of natural or synthetic origin that show an affinity for nicotinic receptors, particularly the α4β2 nAChR subtype, acting as agonist or antagonist ligands. In recent years, we have ventured into in vivo models, finding that the zebrafish appears to be a useful tool, given its versatility and amount of experimental animals, for the search substances with potential pharmacological activity, which allows us to project these selected substances to a rat's model to extend our studies. Currently, we have used the Novel Tank Diving Test (NTT) paradigm as an anxiety or stress model and a Conditioning Place Preference model, similar to one used in rats, to generate a behavior profile in zebrafish, which allowed us to discover new substances with a potential therapeutic effect against nicotine addiction and ethanol consumption.

Autores: Iturriaga-Vásquez P.
Afiliación: Laboratorio de Farmacología Molecular y Química Medicinal, Depto. De Cs Químicas y RRNN, Fac. De Ingeniería y Ciencias, Universidad de La Frontera
Área de la Farmacología: Neuropharmacology
Dirección de Correo: patricio.iturriaga@ufrontera.cl

3.

INCORPORACIÓN / INCORPORATIONS

PRIMER INFORME SOBRE LA SÍNTESIS DE COMPLEJOS DE PD(II) MEDIANTE LA ADICIÓN DE MICHAEL: ACTIVIDAD ANTICANCERÍGENA MEDIANTE APOPTOSIS Y ESTUDIOS DEL MECANISMO DE ACOPLAMIENTO COMO INHIBIDORES DE OBJETIVOS MÚLTIPLES DEL SARS-COV-2. First report on synthesis of Pd(II) complexes via Michael addition: Anticancer activity via apoptosis and mechanistic studies through docking as multi-target inhibitors of SARS-CoV-2.

Metal complexes have numerous applications in the current era, particularly in the field of pharmaceutical chemistry and catalysis. A novel synthetic approach for the same is always a beneficial addition to the literature. Henceforth, for the first time, we report the formation of three new Pd(II) complexes through the Michael addition pathway. Chromone-based thiosemicarbazone ligands and Pd(II) complexes were synthesized and characterized by analytical and spectroscopic tools. The Michael addition pathway for the formation of complexes was confirmed by spectroscopic studies. The distorted square planar structure of complexes was confirmed by single crystal X-ray diffraction. The complexes were subjected to DNA and BSA binding studies. The complex with cyclohexyl substituent on the terminal N of thiosemicarbazone showed the highest binding efficacy towards these biomolecules, which was further understood through molecular docking studies. The anticancer potential of these complexes was studied preliminarily using MTT assay in cancer and normal cell lines along with the benchmark drugs (cisplatin, carboplatin, and gemcitabine). It was found that complex 3 was highly toxic to MDA-MB-231 and AsPC-1 cancer cells with IC50 values of 0.5 and 0.9 µM, respectively, and more efficient than the standard drugs. The programmed cell death mechanism of the complexes in MDA-MB-231 cancer cells was confirmed. Further, the complexes induced apoptosis via ROS-mediated mitochondrial signalling pathway. Conveniently, all the complexes showed less toxicity (≥50 µM) against the MCF-10a normal cell line. Molecular docking studies were performed with VEGFR2, EGFR, and SARS CoV-2 main protease to illustrate the binding efficiency of the complexes with these receptors. To our surprise, the binding potential of the complexes with SARS CoV-2 main protease was higher than that of chloroquine and hydroxychloroquine.

Autores: Haribabu, J.1; Irina Cassandra, R. J.1; Mariel Catalina, M. G. 1; Matías Ignacio, C. O.1; Ester Antonia, H.C. 1; Rocío Carolina, G. R.1; Damaris Belén Z. Z. 1; Krishna Marlen A. C. 1; Iván Ignacio S. P. 1; Ricardo Joaquín, R. M. 1; Camilo Ignacio C. M. 1; Echeverría C.1
Afiliación: Bioinorganic Medicinal Chemistry Laboratory, Faculty of Medicine, Universidad de Atacama.
Área de la Farmacología: Chemotherapy
Dirección de Correo: jebiti.haribabu@uda.cl
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4.

ASOCIACIÓN ENTRE VARIANTES GENÉTICAS Y LA RESPUESTA A LA QUIMIOTERAPIA CITOTÓXICA EN PACIENTES CON NEOPLASIAS HEMATOLÓGICAS. PRESENTACIÓN DE LÍNEA DE INVESTIGACIÓN. Association between genetic variants and response to cytotoxic chemotherapy in patients with hematological malignancies. Presentation of research line.

Las neoplasias hematológicas son prevalentes en adultos y niños. El tratamiento con quimioterapia posee frecuentes reacciones adversas (RAM) con consecuencias clínicas y económicas tanto para el paciente como para el sistema de salud. La genética puede podría predecir la susceptibilidad a RAM, que podrían poner en riesgo la vida de los pacientes. Metodología: Esta línea de investigación se basa en estudios clínicos de seguimiento longitudinal, para establecer una relación entre la presencia de RAM y variantes asociadas a la farmacocinética y farmacodinamia de antineoplásicos. Se utilizaron técnicas de biología molecular como PCR-RFLP y real time – PCR. Fueron reclutados pacientes adultos con neoplasias hematológicas como leucemias y linfomas y pacientes pediátricos con leucemia linfoblástica aguda. La determinación de reacciones adversas fue obtenida a partir del seguimiento prospectivo de los pacientes y de la ficha clínica de cada uno, así como exámenes de laboratorio y registros de farmacia. Se utilizaron métodos estadísticos como regresión logística multivariada y análisis de sobrevida con curvas de

Kaplan-Meier y regresión de Cox para determinar la asociación entre la genética y la toxicidad de la quimioterapia. Resultados: Se encontraron asociaciones entre la genética y el recuento absoluto de neutrófilos, resultado que fue publicado en la revista Pharmacogenomics and Personalized Medicine. También se desarrolló un algoritmo predictivo para la asociación con infecciones, el cual fue publicado en la revista Frontiers in Pharmacology. Los hallazgos realizados en la última cohorte de pacientes pediátricos serán publicados a finales del año 2023, pero indican una influencia de la genética en el inicio de la neutropenia. Conclusiones: La farmacogenómica es una disciplina con amplio desarrollo actual. La implementación en la práctica clínica necesita resultados obtenidos localmente. La genética se asocia a la respuesta a la quimioterapia en pacientes con neoplasias hematológicas. Estos hallazgos servirán para optimizar y personalizar las terapias oncológicas.

Autores: Matías F. Martínez
Afiliación: Departamento de Ciencias y Tecnología Farmacéuticas, Facultad de Ciencias Químicas y Farmacéuticas, Universidad de Chile
Área de la Farmacología: Pharmacogenomics
Dirección de Correo: matias.martinez@ciq.uchile.cl
Agradecimientos: Sociedad Chilena de Pediatría. Universidad de Chile